AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of claims:

1. (previously presented) A method of forecasting a pharmacokinetic parameter of a lipid A analog as an aggregate structure in solution or in an injection preparation, wherein said aggregate structure in solution or injection preparation contains a lipid A analog or a pharmacologically acceptable salt thereof, said method comprising

measuring at least one of membrane fluidity and circular dichroism of the solution or the injection preparation;

preparing a plurality of lots of solutions, each solution having a unique, known value of said pharmacokinetic parameter;

measuring the membrane fluidity or circular dichroism of said plurality of lots of solutions;

preparing a graphical correlation for said plurality of lots of solutions, said correlation being between the

membrane fluidity or circular dichroism and said unique, known value of said pharmacokinetic parameter.

2. (canceled).

3. (previously presented) The method according to claim 1, wherein quality evaluation is conducted in order to obtain an injection preparation exhibiting a constant pharmacokinetic parameter.

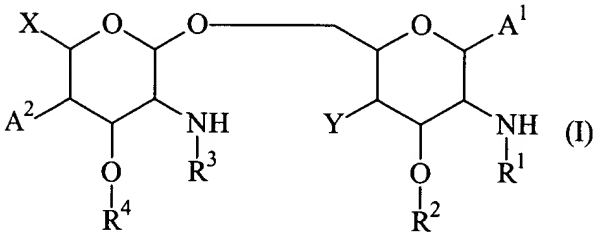
4. (previously presented) The method according to claim 1, which is conducted during preparation of the injection preparation.

5. (previously presented) The method according to claim 1, wherein the membrane fluidity is measured by a fluorescence probe method which uses, as parameters, at least one of order parameter (S), fluorescence polarity (P) and fluorescence anisotropy (r).

6. (previously presented) The method according to claim 1, wherein the injection preparation further contains aggregates having a diameter not greater than 30 nm, and is prepared by dissolving the lipid A analog or a pharmacologically acceptable salt thereof in an alkaline aqueous solution and then adding a buffer thereto.

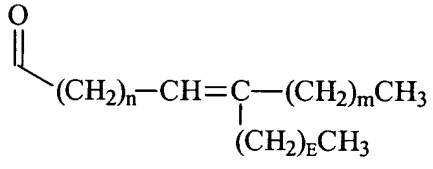
7. (previously presented) The method according to claim 1, wherein the injection preparation is an aqueous injection or freeze-dried preparation.

8. (previously presented) The method according to claim 1, wherein the lipid A analog or a pharmacologically acceptable salt thereof is a compound represented by the following formula (I):

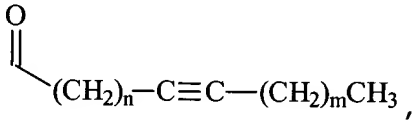


(I)

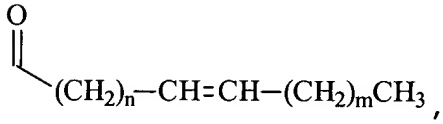
wherein at least one of R^1, R^2, R^3 and R^4 is



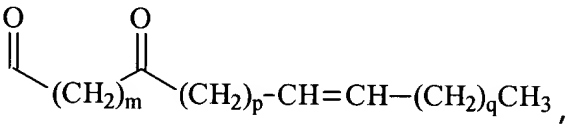
,



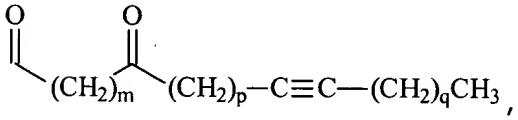
,



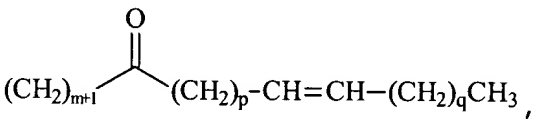
,



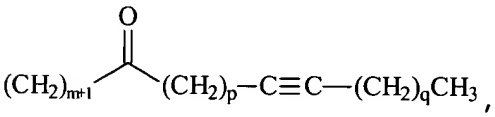
,



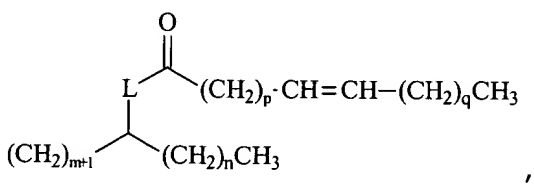
,



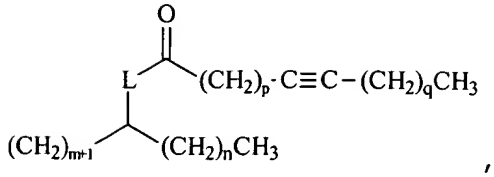
,

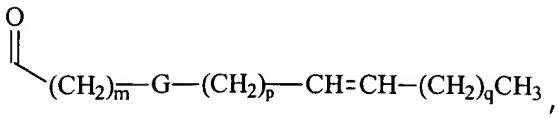


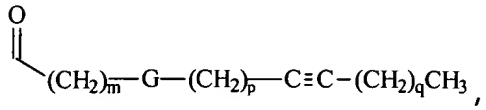
,

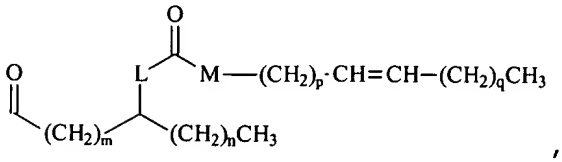


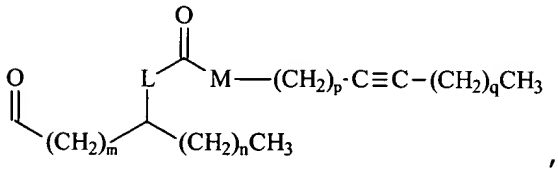
,

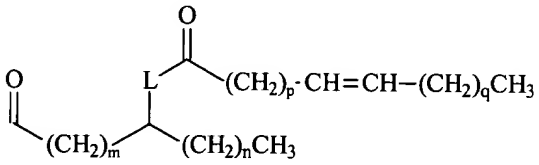


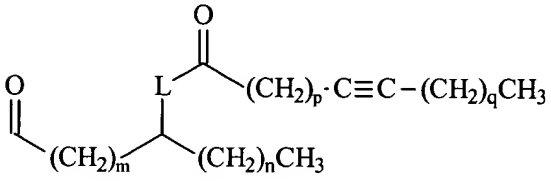
,


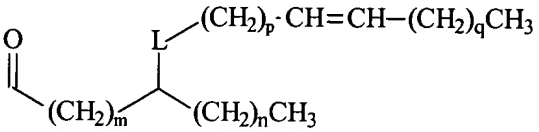
,


,


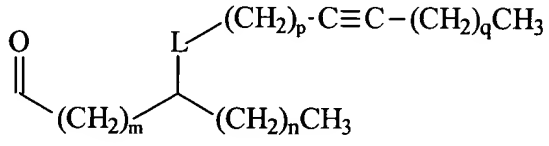
,


,


,


,


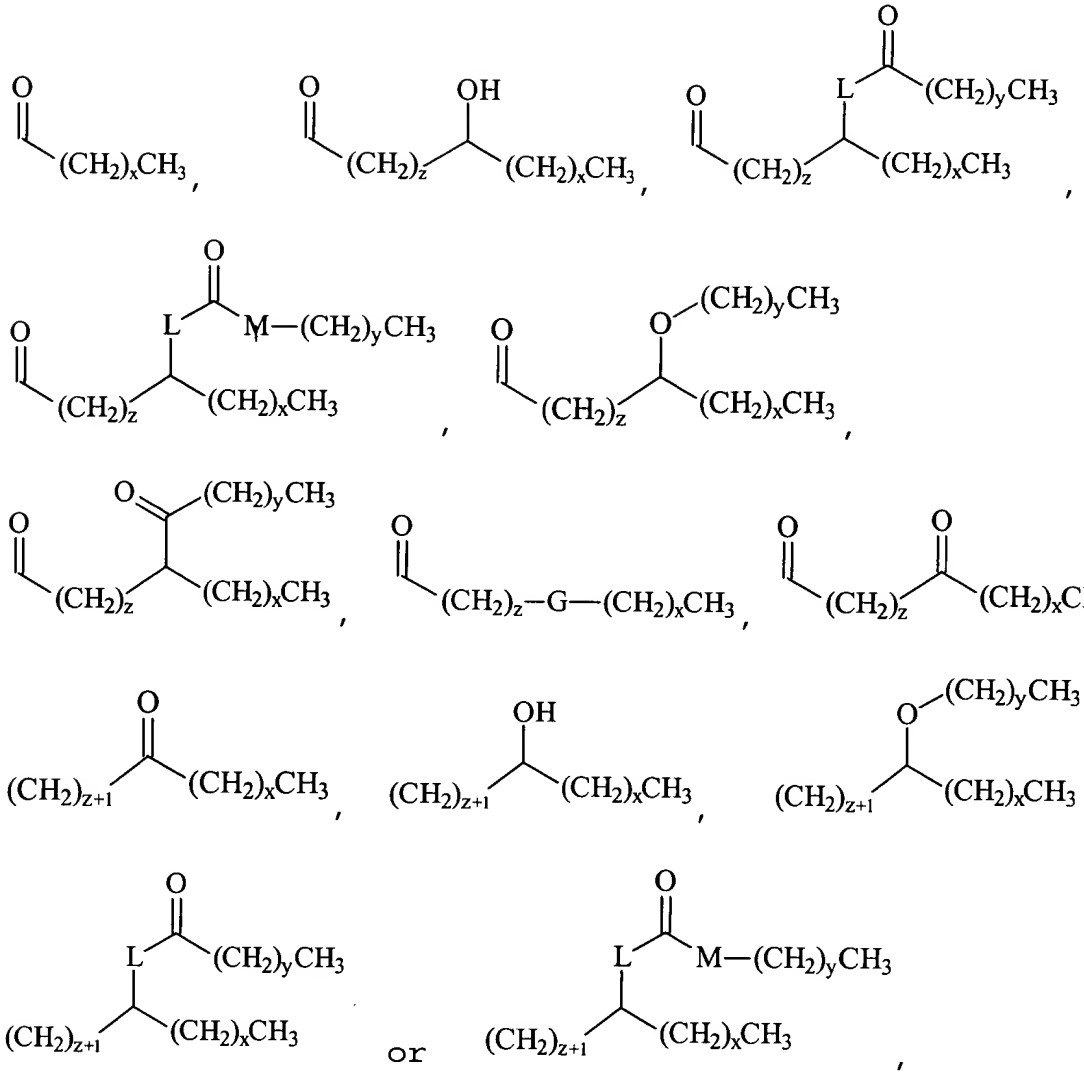
,

or 

,

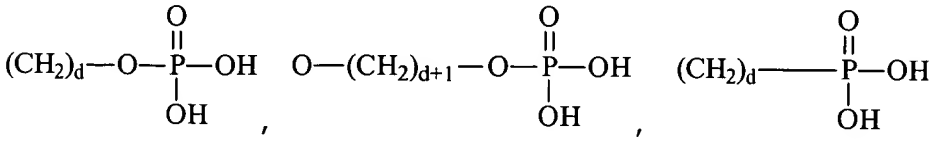
wherein each L is O, N or C; each M is O or N; each E independently is an integer of 0 to 14; each G independently is N, O, S, SO or SO_2; each m independently is an integer of 0 to 14; each n independently is an integer of 0 to 14; each p independently is an integer of 0 to 10; each q independently is an integer of 0 to 10,

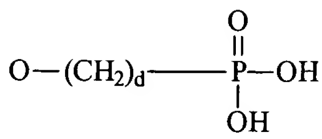
the rest of R^1, R^2, R^3 and R^4 are, independently of one another,

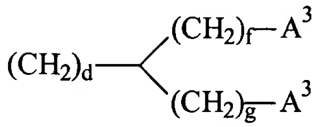
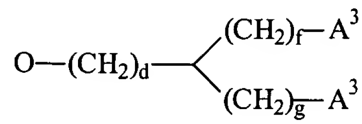


wherein each L is O, N or C; each M is O or N; each x independently is an integer of 0 to 14; each y independently is an integer of 0 to 14; each z independently is an integer of 0 to 10; each G independently is N, O, S, SO or SO_2,

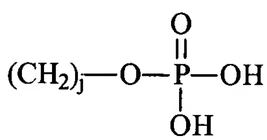
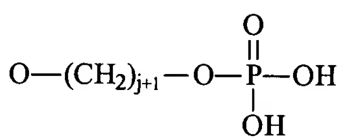
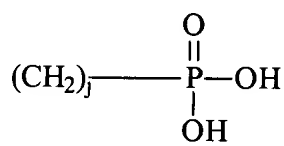
A^1 and A^2 are, independently of one another, H, OH, OCH_3,

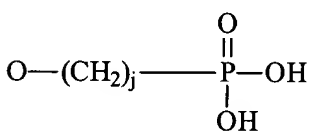


 , $(CH_2)_d—CO_2H$, $O—(CH_2)_d—CO_2H$,

 or  ,

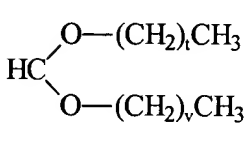
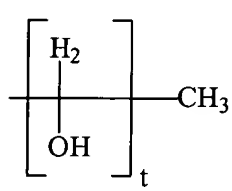
wherein each d independently is an integer of 0 to 5; each f independently is an integer of 0 to 5; each g independently is an integer of 0 to 5; each A^3 independently is

 ,  ,  ,

 , $(CH_2)_j—CO_2H$ or $O—(CH_2)_j—CO_2H$,

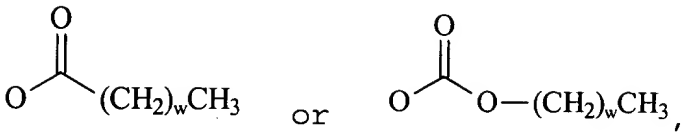
wherein each j independently is an integer of 0 to 14,

X is H, $(CH_2)_tCH_3$, $(CH_2)_tOH$, $(CH_2)_tO(CH_2)_vCH_3$, $(CH_2)_tOPO(OH)_2$, $(CH_2)_t\text{-}CH{=}CH\text{-}(CH_2)_vCH_3$, $(CH_2)_t\text{-}O\text{-}R^5$,

 or 

wherein t and v, are independently of one another, an integer of 0 to 14; R^5 is any of the above definitions of R^1 to R^4,

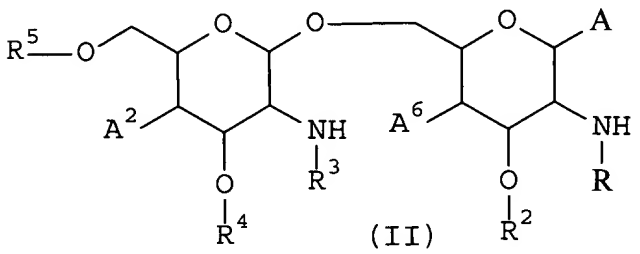
Y is H, OH, $O(CH_2)_wCH_3$, a halogen atom,



wherein w is an integer of 0 to 14,

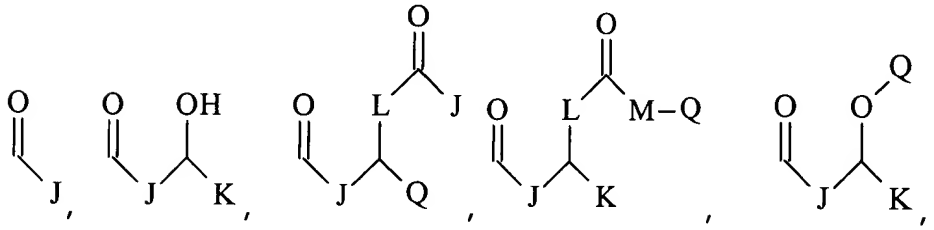
or a pharmacologically acceptable salt thereof.

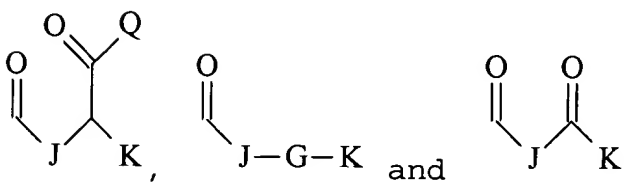
9. (previously presented) The method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (II):



(II)

wherein R^1 is a group selected from the groups consisting of



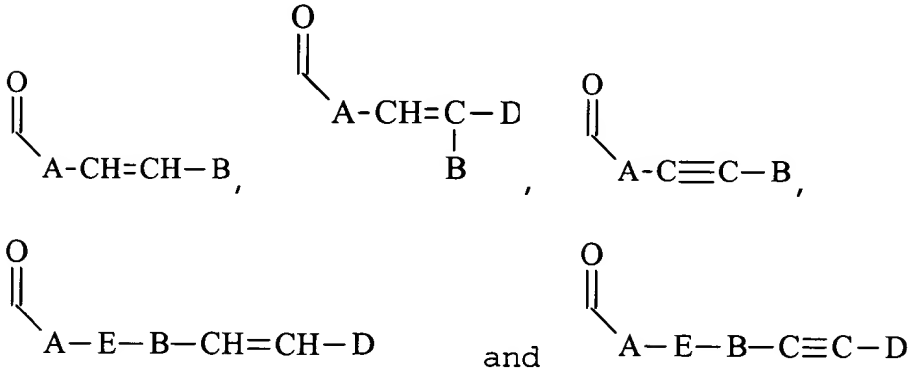


and

wherein J, K and Q are each a linear or branched alkyl group of 1 to 15 carbon atoms; L is O, NH_2 or CH_2; M is O or NH; G is NH, O, S, SO or SO_2,

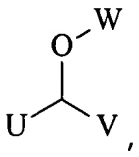
R^2 is a linear or branched alkyl group of 5 to 15 carbon atoms,

R^3 is a group selected from the groups consisting of



wherein E is N, O, S, SO or SO_2; A, B and D are each a linear or branched alkyl group of 1 to 15 carbon atoms,

R^4 is a group selected from the groups consisting of a linear or branched alkyl group of 4 to 20 carbon atoms and



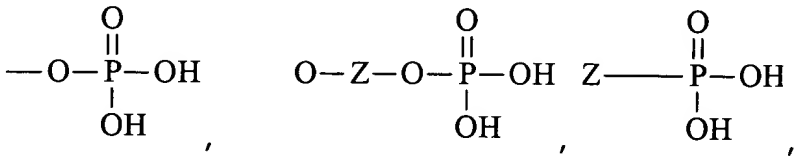
wherein U and V are each a linear or branched alkyl group of 2 to 15 carbon atoms; W is a hydrogen atom or a linear or branched alkyl group of 1 to 5 carbon atoms,

R^5 is a group selected from the groups consisting of a hydrogen atom, J', -J'-OH, -J'-O-K', -J'-O-K'-OH and

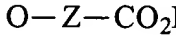
-J'-O-PO(OH)$_2$, wherein J' and K' are each a linear or branched alkyl group of 1 to 5 carbon atoms,

R^6 is a group selected from the groups consisting of a hydroxyl group, a halogen atom, an alkoxy group of 1 to 5 carbon atoms, and an acyloxy group of 1 to 5 carbon atoms,

A^1 and A^2 independently are each a group selected from the groups consisting of



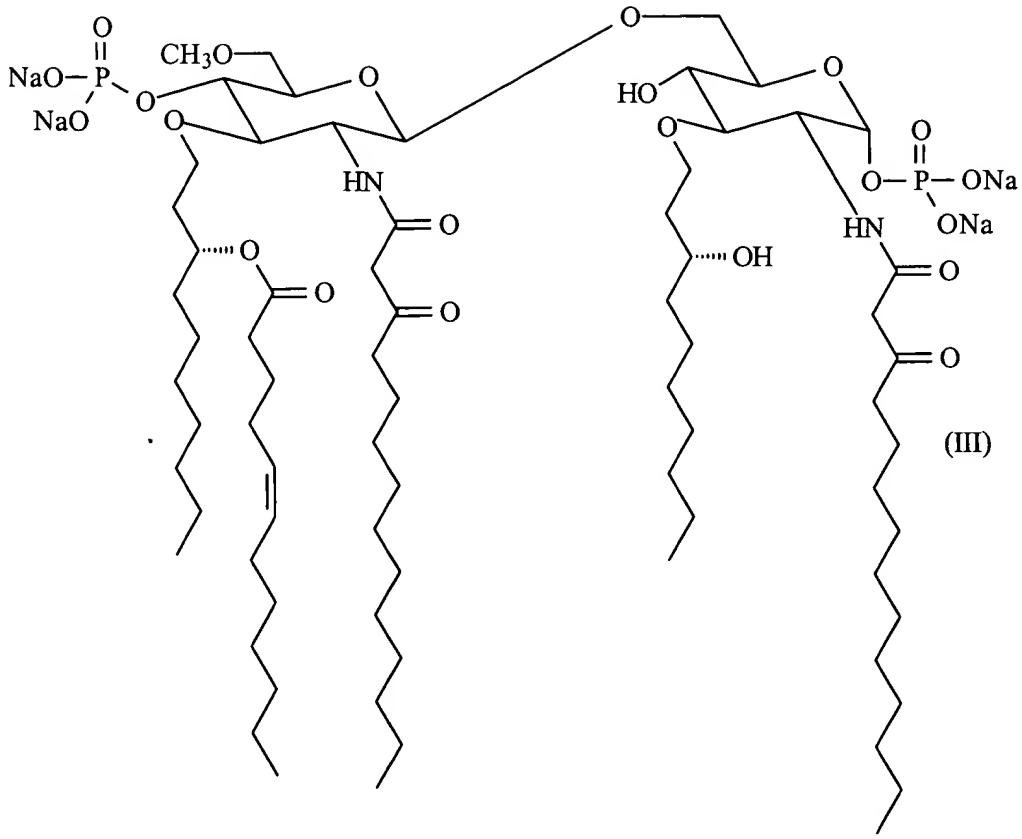
OH,

and  ,

wherein Z is a linear or branched alkyl group of 1 to 10 carbon atoms,

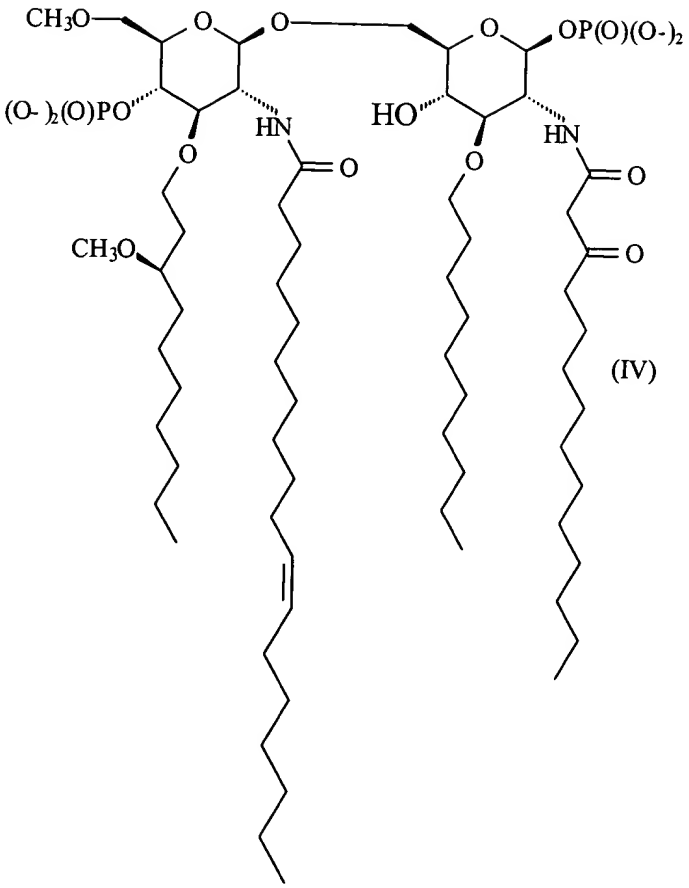
or a pharmacologically acceptable salt thereof.

10. (previously presented) The method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (III):



(III)

11. (previously presented) The method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (IV):



(IV)

12. (previously presented) The method according to claim 1, wherein the lipid A analog or a pharmacologically acceptable salt thereof has an aggregate structure in endoplasmic reticulum of lipid biomolecular membrane or micelle.

Please add the following new claims:

13. (new) A method of forecasting a pharmacokinetic parameter of a lipid A analog as an aggregate structure in solution or in an injection preparation, wherein said aggregate structure in solution or injection preparation contains a lipid

A analog or a pharmacologically acceptable salt thereof, said method comprising

measuring at least one of membrane fluidity and circular dichroism of the solution or the injection preparation;

preparing a plurality of lots of solutions, each solution having a unique, known value of said membrane fluidity or circular dichroism;

measuring the pharmacokinetic parameter of said plurality of lots of solutions;

preparing a graphical correlation for said plurality of lots of solutions, said correlation being between the pharmacokinetic parameter and said unique, known value of membrane fluidity or circular dichroism.

14. (new) The method according to claim 13, wherein quality evaluation is conducted in order to obtain an injection preparation exhibiting a constant pharmacokinetic parameter.

15. (new) The method according to claim 13, which is conducted during preparation of the injection preparation.

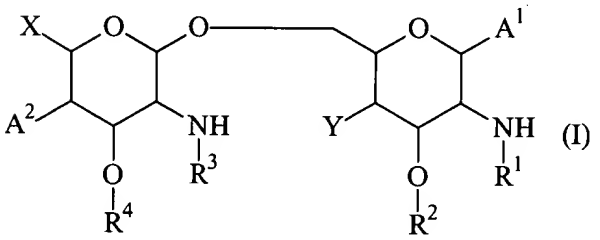
16. (new) The method according to claim 13, wherein the membrane fluidity is measured by a fluorescence probe method

which uses, as parameters, at least one of order parameter (S), fluorescence polarity (P) and fluorescence anisotropy (r).

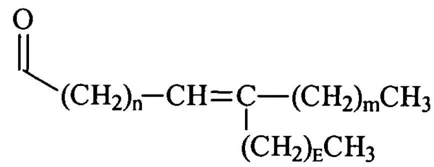
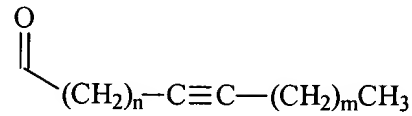
17. (new) The method according to claim 13, wherein the injection preparation further contains aggregates having a diameter not greater than 30 nm, and is prepared by dissolving the lipid A analog or a pharmacologically acceptable salt thereof in an alkaline aqueous solution and then adding a buffer thereto.

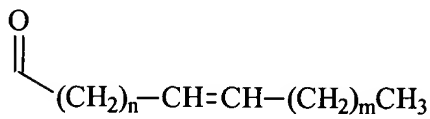
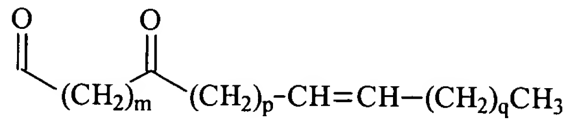
18. (new) The method according to claim 13, wherein the injection preparation is an aqueous injection or freeze-dried preparation.

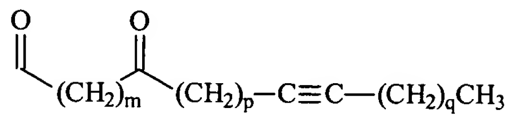
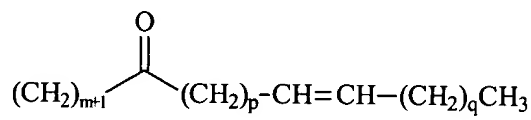
19. (new) The method according to claim 13, wherein the lipid A analog or a pharmacologically acceptable salt thereof is a compound represented by the following formula (I):

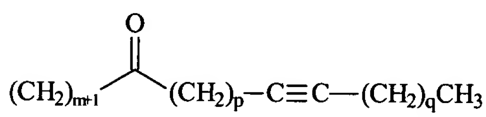
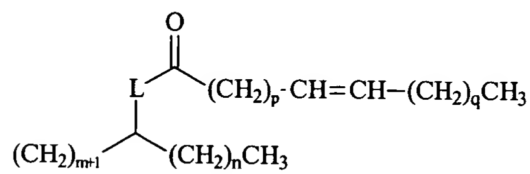


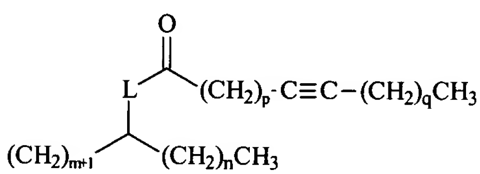
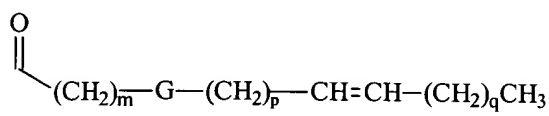
wherein at least one of R^1, R^2, R^3 and R^4 is

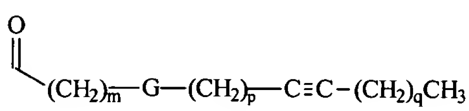
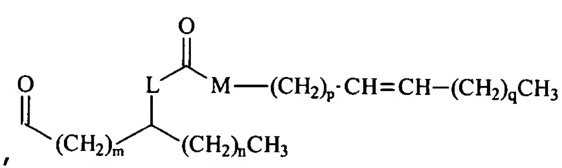
 ,
 ,

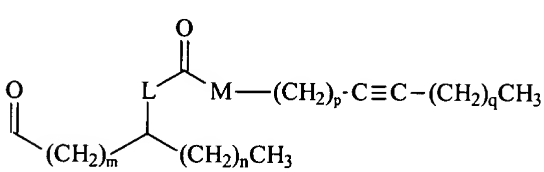
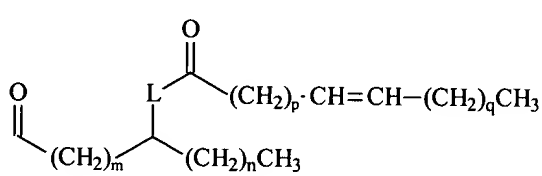
 ,
 ,

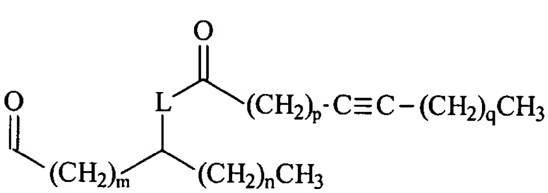
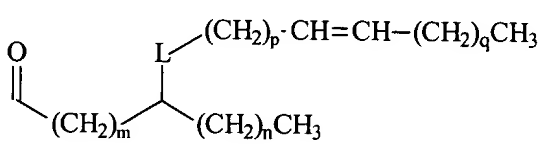
 ,
 ,

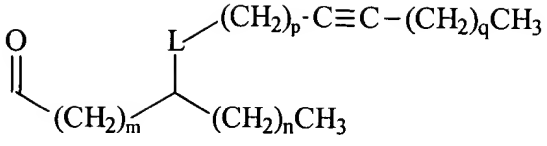
 ,
 ,

 ,
 ,

 ,
 ,

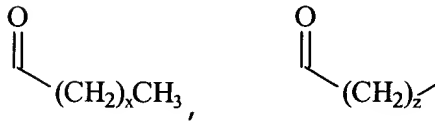
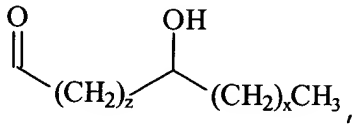
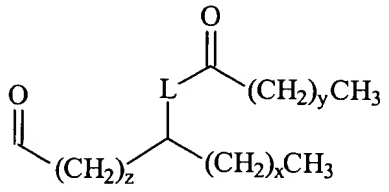
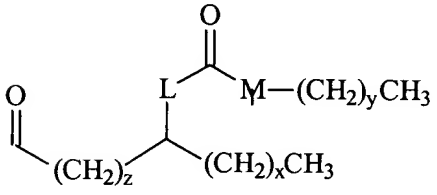
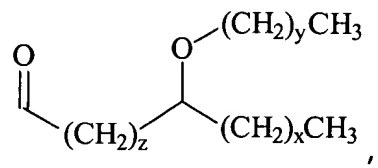
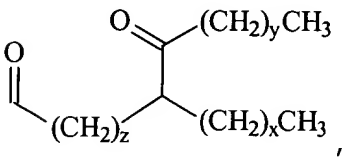
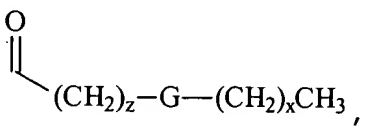
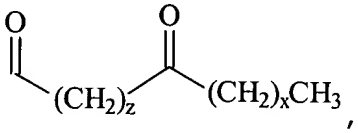
 ,
 ,

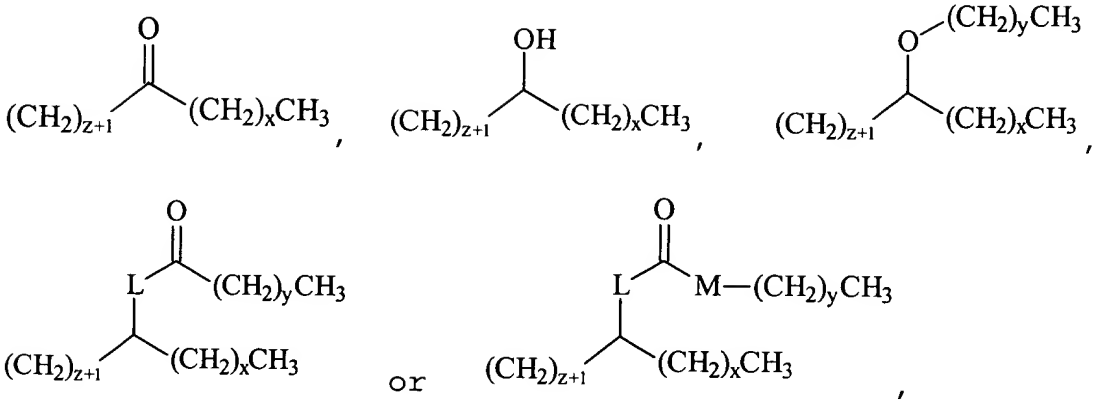
 ,


or  ,

wherein each L is O, N or C; each M is O or N; each E independently is an integer of 0 to 14; each G independently is N, O, S, SO or SO_2; each m independently is an integer of 0 to 14; each n independently is an integer of 0 to 14; each p independently is an integer of 0 to 10; each q independently is an integer of 0 to 10,

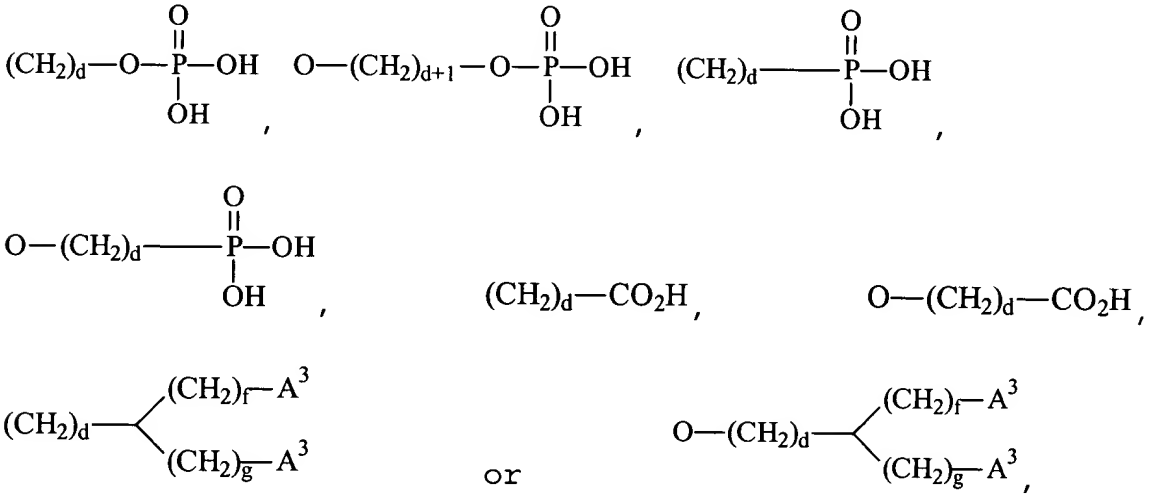
the rest of R^1, R^2, R^3 and R^4 are, independently of one another,

 ,
 ,
 ,
 ,
 ,
 ,
 ,
 ,

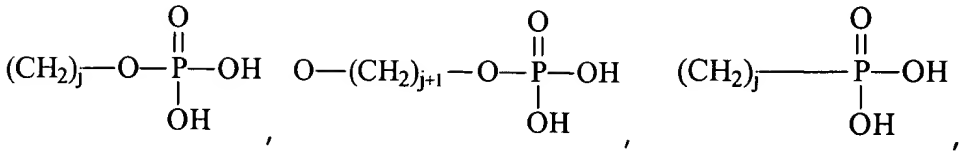


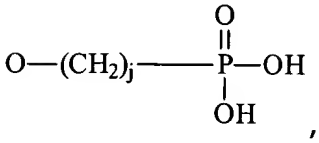
wherein each L is O, N or C; each M is O or N; each x independently is an integer of 0 to 14; each y independently is an integer of 0 to 14; each z independently is an integer of 0 to 10; each G independently is N, O, S, SO or SO_2,

A^1 and A^2 are, independently of one another, H, OH, OCH_3,



wherein each d independently is an integer of 0 to 5; each f independently is an integer of 0 to 5; each g independently is an integer of 0 to 5; each A^3 independently is

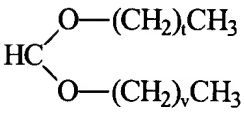




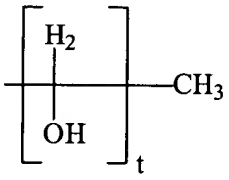
or

wherein each j independently is an integer of 0 to 14,

X is H, $(CH_2)_tCH_3$, $(CH_2)_tOH$, $(CH_2)_tO(CH_2)_vCH_3$, $(CH_2)_tOPO(OH)_2$, $(CH_2)_t$-CH=CH-$(CH_2)_vCH_3$, $(CH_2)_t$-O-R^5,

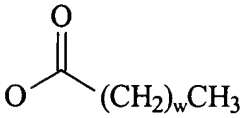


or

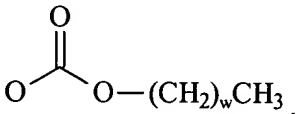


wherein t and v, are independently of one another, an integer of 0 to 14; R^5 is any of the above definitions of R^1 to R^4,

Y is H, OH, $O(CH_2)_wCH_3$, a halogen atom,



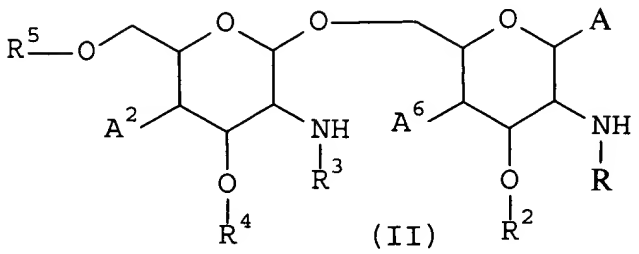
or



wherein w is an integer of 0 to 14,

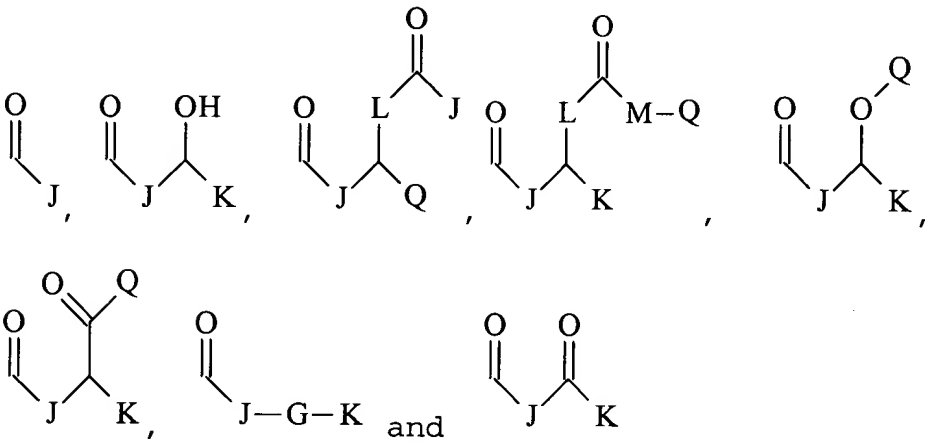
or a pharmacologically acceptable salt thereof.

20. (new) The method according to claim 13, wherein the lipid A analog is a compound represented by the following formula (II):



(II)

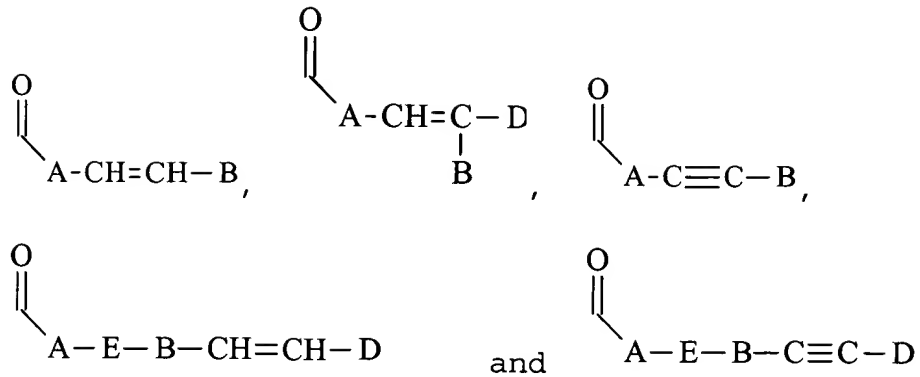
wherein R^1 is a group selected from the groups consisting of



wherein J, K and Q are each a linear or branched alkyl group of 1 to 15 carbon atoms; L is O, NH_2 or CH_2; M is O or NH; G is NH, O, S, SO or SO_2,

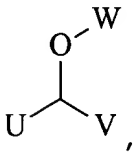
R^2 is a linear or branched alkyl group of 5 to 15 carbon atoms,

R^3 is a group selected from the groups consisting of



wherein E is N, O, S, SO or SO_2; A, B and D are each a linear or branched alkyl group of 1 to 15 carbon atoms,

R^4 is a group selected from the groups consisting of a linear or branched alkyl group of 4 to 20 carbon atoms and



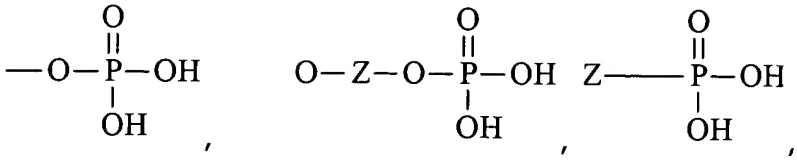
wherein U and V are each a linear or branched alkyl group of 2 to 15 carbon atoms; W is a hydrogen atom or a linear or branched alkyl group of 1 to 5 carbon atoms,

R^5 is a group selected from the groups consisting of a hydrogen atom, J', -J'-OH, -J'-O-K', -J'-O-K'-OH and -J'-O-$PO(OH)_2$, wherein J' and K' are each a linear or branched alkyl group of 1 to 5 carbon atoms,

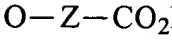
R^6 is a group selected from the groups consisting of a hydroxyl group, a halogen atom, an alkoxy group of 1 to 5 carbon atoms, and an acyloxy group of 1 to 5 carbon atoms,

A^1 and A^2 independently are each a group selected from the groups

consisting of



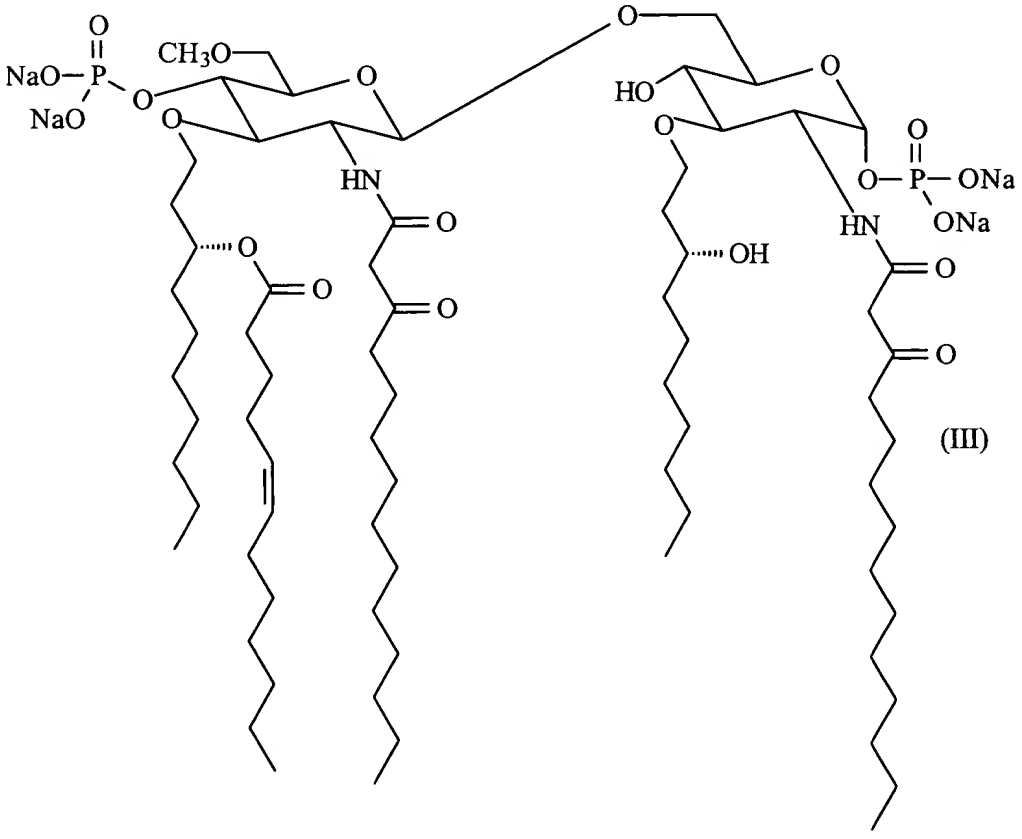
OH,

and  ,

wherein Z is a linear or branched alkyl group of 1 to 10 carbon atoms,

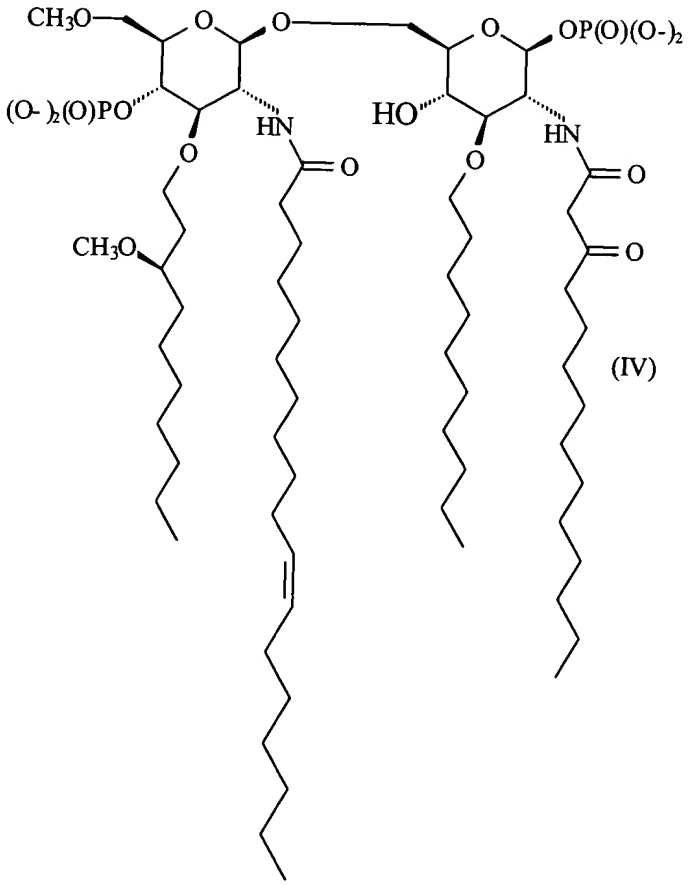
or a pharmacologically acceptable salt thereof.

21. (new) The method according to claim 13, wherein the lipid A analog is a compound represented by the following formula (III):



(III)

22. (new) The method according to claim 13, wherein the lipid A analog is a compound represented by the following formula (IV):



23. (new) The method according to claim 13, wherein the lipid A analog or a pharmacologically acceptable salt thereof has an aggregate structure in endoplasmic reticulum of lipid biomolecular membrane or micelle.